

## **II. Remarks/ Arguments**

Reconsideration of the application in view of the above amendments and the following remarks is requested.

The Examiner has rejected claims 1, 4, 7-8, 12-16, 57-60 and 69 under 35 U.S.C. 112, stating that they fail to comply with the written description requirement.

Applicant has amended the claims to remove any reference to the terms “solvate or hydrate”. The Examiner states that solvates are not well known and accepted modifications to a compound and that a person skilled in the art would not be able to determine, from the direction provided, what compounds would qualify as such. In order to expedite prosecution, Applicant has removed the terms “solvate” and “hydrate” from the claims.

The Examiner has rejected claims 57-60 under 35 U.S.C. 112, first paragraph, stating that the specification, while enabling for inhibiting secretion of vascular endothelial growth factor, does not reasonably provide enablement for treating those who are at risk for developing tumors.

The Examiner states that the applicant has established enablement for treatment of breast cancer and inhibiting VEGF secretion but that the applicant has not enabled treatment of animals who are “at risk”.

While applicant disagrees with the Examiner’s position, as outlined in the previous response, Applicant has removed claim 57 from the pending claim set and has amended claim 58 to be dependent on claim 1. Applicant believes the Examiner’s objection is now overcome since the language of being “at risk of developing” has now been removed from the claims.

### **Claim Rejections- 35 U.S.C.§103(a)**

The Examiner has rejected claims 8, 12-16, 57-60 and 69 under 35 U.S.C. 103(a) as being unpatentable over Roifman et al. (WO 01/79158 A2) in view of Bessette et al. (US 2003/0017215 A1) in further view of Butler et al. (US 5,486,457).

Applicant respectfully disagrees that the subject matter of the pending claims is obvious in light of the cited references. However, in order to expedite prosecution of the application, Applicant has removed these claims from the pending claim set at this time.

The Examiner has further rejected claims 1, 4, 7-8, 12-16, 57-60 and 69 under 35 U.S.C. 103(a) as being unpatentable over Roifman et al. (WO 01/79158 A2) in view of Foekens et al. (Cancer Research, 2001, Vol. 61, pages 5407-5414).

The Examiner states that Roifman et al. teaches the treatment of cancer and the specific structure CR4. However, there is no discussion of VEGF in Roifman et al.

The Examiner states that Foekens et al. teaches that in patients with advanced breast cancer VEGF levels have been found to be elevated. The Examiner then states that a person of ordinary skill in the art would know that breast cancer is a form of cancer and that therefore they would use the compounds of Roifman et al. to treat breast cancer and that patients with breast cancer are in need of inhibiting secretion of VEGF. The Examiner states that the claimed method is therefore suggested and motivated in the prior art.

The pending claims are directed to a method of inhibiting secretion of vascular endothelial growth factor in an animal and a method of inhibiting an effect of vascular endothelial growth factor in an animal in need of such inhibition. The pending claims are all related to the inhibition of vascular endothelial growth factor (VEGF). As stated in the Summary of the Invention section, the present application is directed to the "unexpected discovery" that certain compounds are capable of inhibiting the activity of VEGF. In addition, *in vitro* data is provided to show that the exemplified compounds inhibit VEGF secretion, see Examples 15-18. As stated by the Examiner, the applicant has made a "significant scientific discovery" that VEGF is involved in the mechanism of action in the disclosed compounds.

Applicant respectfully submits that a person skilled in the art would not combine these references to result in Applicant's claimed subject matter, and further that any such combination would not result in the same. Foekens et al. discusses VEGF levels in advanced breast cancer and discusses the possible use of VEGF as a marker in the prediction of poor efficacy of both

tamoxifen and chemotherapy. VEGF is described as being an “independent marker that predicts efficacy” and that knowledge of VEGF levels may help in selecting patient populations for alternative treatments. There is no discussion of the compounds described in Roifman et al. and there is no discussion of VEGF being a target for such compounds. There is also no discussion or teaching of the use of any specific compounds for directly inhibiting secretion of VEGF or inhibiting the effect of VEGF.

Applicant submits that a person skilled in the art reading Roifman et al, which discloses a group of compounds for the treatment of cell proliferation disorders, would not turn to a reference, such as Foekens, which discusses the possible use of a marker, i.e. VEGF, as a predictor of poor efficacy of prior treatments in advanced breast cancer. Since there is no discussion of VEGF in Roifman et al. and no discussion of the compounds of Roifman et al. in Foekens et al, Applicant submits that such references would not be combined and therefore do not render obvious the subject matter of the pending claims.

Applicant respectfully submits, as stated above, that there is no teaching or suggestion, in any of the cited references, of the specific use of the claimed compounds for the inhibition of VEGF. Therefore, although as stated by the Examiner, Roifman teaches, for example, the structure of CR4, there is no discussion of the use of CR4 for the inhibition of VEGF. In addition, there is no discussion of the claimed compounds in Foekens et al.. Applicant therefore, respectfully submits that a person skilled in the art, given the teachings in the cited art, would not be led to the subject matter of the pending claims. Withdrawal of this objection is respectfully requested.

In view of the above remarks, and amendments submitted herewith, the Applicant respectfully submits that independent amended claims 1 and 4 are novel and inventive over the cited art. Further, as the remaining dependent claims are dependent on these independent claims, the Applicant similarly respectfully submits that these claims are novel and inventive over the cited art. The Applicant respectfully requests reconsideration and allowance of the application.

If the Examiner has further concerns, he is encouraged to contact the Applicant's undersigned agent if the Examiner considers that a telephone conference would be of assistance in this matter.

Respectfully submitted,

A handwritten signature in cursive script that reads "James A. Gromada".

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